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Early Life Antibiotic Exposure and its Association with Overweight/Obesity: An Integrative Review of the Literature

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Background & Introduction

- Colonization of human intestinal microbiota begins at or even before birth and continues to develop throughout infancy.
- Establishment and colonization patterns of microbiota result from multiple factors like delivery mode and environmental determinants including birth method, nutrition, hygiene conditions, and the use of antibiotics (Moreira, Teixeira, Peluzio, & Alfenas, 2012).
- Antibiotics are known disruptors of the composition of intestinal microbiota.
- Antibiotics have been used for decades in the animal farming industry to promote faster growth in animals, so it is logical to think that the same mechanism may be at work in the human model.
- A disrupted metabolism is directly related to increased weight gain, causing the body to extract and store more adipose tissue than what is necessary for bodily function, regardless of caloric intake (Cox and Blaser, 2015).

Purpose

The aim of this integrative literature review was to identify factors associated with greater incidence or effects of antibiotic exposure during infancy and to examine the connection between early life antibiotic exposure and later in life overweight/obesity.

Research Questions

The following questions were addressed:

- What are the factors associated with greater incidence of or effect of antibiotic exposure during infancy?
- Is early life antibiotic exposure associated with a higher risk of overweight/obesity?

Methods

- This study utilized an integrative literature review to identify what is known or unknown, up to November 2016, about the factors associated with antibiotic exposure during infancy and the connection between early life antibiotic exposure and overweight/obesity.
- This specific design, outlined by Whittemore and Knafl (2005) allowed selected literature on the topic to be analyzed and compared in order to further develop an understanding of the topic.
- Sources generated from two databases: Cumulative Index of Nursing and Allied Health (CINAHL) and PubMed-NCBI.
- The Boolean/Phrase search mode was utilized and included combinations of the following terms: *infant*, *antibiotic*, *exposure*, *obesity*, and *body mass*.
- Inclusion criteria used to choose studies and other relevant reviews included the following points:
 - A population of human subjects (not animal models)
 - Published between 2008-2016
 - Documentation of effects of early life antibiotic administration on body mass/obesity rates
- Articles that did not meet the above criteria, as well as articles that were repeated, were excluded.
- The final CINAHL database search returned 17 results. Of these, 5 were chosen for inclusion based on inclusion criteria.
- The final PubMed search returned 18 results, 5 were repeats of the CINAHL search, and a total of 3 articles were chosen for inclusion in the literature review. In total, 8 articles were chosen for review from CINAHL and PubMed.
- Two opinion pieces/reviews were ultimately included in the research grid so that secondary sources could be accessed from the articles for the integrative literature review.

Results

FACTORS ASSOCIATED WITH INCIDENCE OF OR EFFECTS OF ANTIBIOTIC EXPOSURE

- Three factors were identified as being associated with an increased incidence of antibiotic exposure or with more pronounced overweight effects of antibiotic exposure.
- Significant factors included:
 - maternal related factors
 - biological factors
 - type of antibiotic given

ASSOCIATION BETWEEN ANTIBIOTIC EXPOSURE AND RISK FOR OVERWEIGHT/OBESITY

- The six quantitative studies reviewed each reported a link between antibiotic exposure in early life and risk for overweight/obesity at some point during childhood (Ajslev et al., 2011; Azad et al., 2014; Bailey et al., 2014; Murphy et al., 2014; Saari et al., 2015; Trasande et al., 2012).
- These studies point out an association, not a causal link between antibiotic exposure and overweight/obesity.
- Cumulatively, these epidemiological studies looked at data from tens of thousands of subjects from long periods of time and found that an association indeed exists.

Discussion

Antibiotics are frequently used to treat infants and children as well as prophylactically during the perinatal period (Cox and Blaser, 2015). Much is still unknown or inconclusive regarding the function of intestinal microbiota in health and disease states, especially that of the infant and young child. However, given the mechanism of action of antibiotics, the potential for disruption of intestinal microbiota is logical.

Previous murine studies have shown that antibiotics increase body fat mass in mice, which is assumed to be a result of changes to intestinal microbiota by antibiotic agents. These changes are thought to increase the energy-harvesting ability of intestinal microbiota in mice (Cho et al., 2006 and Turnbaugh et al., 2006). A similar mechanism of action may be occurring in humans whose intestinal microbiota is altered by the effects of antibiotics.

Limitations

- This review was not intended to examine other early-life factors that may contribute to prevalence of obesity or overweight.
- Not all studies chosen for review measured potential confounding factors that may increase or influence risk for obesity or overweight.
- Studies were selected based on literature search strategies and inclusion/exclusion criteria as outlined above, however these criteria could also serve as a limitation.

Nursing Implications & Conclusion

NURSING IMPLICATIONS

Prevention of obesity from a public health standpoint would remove significant burden from the healthcare system, potentially saving many lives and billions of dollars annually. Infancy may be a critical period during which efforts should be focused to prevent obesity. Better stewardship in prescribing antibiotics and more comprehensive patient teaching could help cut down on the overuse of antibiotics, and the potentially harmful long-term effects. Nurses can play a role in research, patient education, and patient advocacy.

CONCLUSION

Disruption of the intestinal microbiota by early or repeated exposure to antibiotics in infancy could lead to obesity later in life, as evidenced by these five large cohort, multicenter studies. It is important to work to understand the additional factors, related or independent, that may contribute to later in life obesity. Antibiotics are often over-prescribed and misused, especially for childhood infections. Modifiable factors, including but not limited to the prudent use of antibiotics in infants, should continue to be identified through research and literature review.

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